

These amendments are made without prejudice and are not to be construed as abandonment of the previously claimed subject matter. For the convenience of the Examiner, a complete set of the presently pending claims is provided in Appendix B attached hereto.

REMARKS

Entry of the foregoing amendments and reconsideration and reexamination of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112 and in light of the remarks which follow, are respectfully requested.

At the outset, Applicants thank Examiners Wang and Wessendorf for their time on Monday, March 24, 2003 to discuss the outstanding Restriction Requirement, the new claims, and the proposed interference with U.S. Patent No. 6,479,258 ("the '258 patent") issued to Short.

Applicants have amended the specification to correct several inadvertent typographical errors. First, the specification has been amended to correct a typographical error in the paragraph beginning on page 1, line 6 under the header entitled "CROSS-REFERENCE TO RELATED APPLICATIONS" that was added by amendment at the time of filing as shown in the Transmittal Form filed with the application on November 28, 2000. The paragraph added by amendment at the time of filing included a typographical error in the serial number of the provisional application of the priority claim. Although the priority claim was properly stated and made on the November 28, 2000 Transmittal Form, the amended paragraph proposed for inclusion incorrectly showed the priority provisional application serial number as 60/074; the correct serial number is 60/074,294, as shown elsewhere on the Transmittal Form. Second, Applicants have amended the specification to delete the header "STATEMENT REGARDING GOVERNMENT SUPPORT" on page 1, line 5 and the paragraph immediately there under beginning on page 1, line 6. This header and paragraph were inadvertently included in the specification. None of these amendments introduces any new matter.

I. STATUS OF THE CLAIMS.

Applicants have canceled claims 1-46 without disclaimer of or prejudice as to the subject matter contained therein. Applicants reserve the right to file a continuation or divisional application on the canceled subject matter.

Applicants have added new claims 47 and 48. Support for claims 47 and 48 can be found throughout the specification, including as set forth in Appendix C attached hereto. Accordingly, no prohibited new matter is believed to have been introduced by entry of this amendment.

II. RESPONSE TO THE RESTRICTION REQUIREMENT AND SPECIES ELECTION REQUIREMENT.

Restriction Requirement.

In the Office Action, the Examiner restricted originally pending claims 1-46 under 35 U.S.C. § 121, requiring Applicants to elect one of the following claim groups for prosecution in the present application:

- I. Claims 1-40, "drawn to a method for obtaining a polynucleotide that has a modulatory effect on an immune response," classified in Class 435, subclass 6.
- II. Claims 41-46; "drawn to a method of obtaining a polynucleotide that encodes an accessory molecule," classified in Class 435, subclass 6.

Office Action, page 2.

Applicants believe the restriction requirement is moot in view of the addition of new claims 47-48 and cancellation of all pending claims 1-46. To the extent the restriction requirement applies to original claims 1-46 and/or new claims 47-48, Applicants respectfully traverse the requirement for at least the following reasons and preserve the right to petition the requirement in the event it is made final.

M.P.E.P. § 803 states that an application may be properly restricted to one or more claimed inventions **only** if (1) the inventions are independent or distinct as claimed, **and** (2) search and examination of the entire application cannot be made without serious burden on the Examiner. Thus, even if appropriate reasons exist for requiring restriction, such a requirement should not be made unless there is a serious burden on the Examiner to search and examine all of the claims in a single application. A serious burden may be *prima facie* established by presenting an appropriate and sufficient explanation of separate classification of the inventions, separate status in the art of the inventions when classifiable together, or a different field of search for one of the distinct subjects.

In the present case, Applicants respectfully submit the Examiner has not *prima facie* established by sufficient evidence or explanation that it would constitute a serious or undue burden to conduct a search and examination of all of the previously pending claims of Groups I and II in a single application. No explanation as to the serious burden posed by search or examination of all of the claims was provided in the Office Action. Moreover, the claims of Groups I and II both were classified in the same class (435) and the same subclass (6), which strongly suggests that no burdensome search would exist if the claims were rejoined. *See* M.P.E.P. § 803.01. Notably, where the subject matter of each claim group is classified identically, an appropriate explanation must be provided as to why the inventions corresponding to the groups would be deemed to have separate status in the art or why a different field of search would be required for each invention. *See* M.P.E.P. § 808.02. Neither sufficient explanation nor adequate evidence was provided to establish the inventions of Groups I and II would have separate status in the art or require a different field of search.

Applicants further note that the claims of the '258 patent issued to Short are substantially the same as those of previously pending claims 1-46, and that Short claim 30 is essentially the same as new claims 47 and 48 of the present application. The claims of the '258 patent were not subjected to restriction. The procedural treatment of the '258 patent at least indicates that search and examination of the subject matter of previously pending claims 1-46 would not pose an undue burden on the Examiner.

Accordingly, for at least these reasons, Applicants respectfully request reconsideration of the restriction requirement and rejoinder of all the claims in view of the above.

However, in the event the restriction requirement is maintained and/or found to apply to new claims 47 and 48, Applicants provisionally elect the invention of **Group I with traverse**. New claims 47 and 48 read upon Group I. More specifically, claims 47 and 48 are most similar to now canceled claims 24 and 25, which were designated as belonging to Group I. In the event the restriction is made final, Applicants respectfully reserve the right to petition the Commissioner to review the requirement.

Species Election Requirement.

Applicants believe the election requirement is moot in view of the addition of new claims 47-48 and cancellation of all pending claims 1-46. To the extent the election requirement applies to original claims 1-46 and/or new claims 47-48, Applicants respectfully traverse the requirement for at least the following reasons and preserve the right to petition the requirement in the event it is made final.

With the election of Group I, Applicants were further required to elect a single species from one of the following Subgroups: (1) "Method of creating a library (e.g., claims 1 and 4);" (2) "Method of screening;" and (3) "Composition comprising of the optimized polynucleotide and genetic vaccine vector or method of administering said composition (e.g., claims 4 and 15)." *Id.*, page 3.

With the election of Subgroup 1 ("method of producing"), Applicants were further required to elect one of the following: (a) DNA shuffling; (b) error-prone PCR; (c) oligonucleotide-directed mutagenesis; (d) uracil-mediated mutagenesis; (e) repair-deficient host mutagenesis; (d) [*sic*] method of producing an optimized polynucleotide by recombining a plurality of n. a. as recited in claim 5; or (f) method of producing an optimized polynucleotide by recombining with a further nucleic acid as recited in claim 6. *Id.*, pages 4-5.

With the election of Subgroup 2 ("screening method"), Applicants were further required to elect one of the following: (A) recombinant interaction with a cellular receptor (claim 7) or non-cellular receptor; (B) screening wherein the encoded polypeptides [*sic*]: (i) produced as fusion displayed on the surface of a bacteriophage (claim 12), (ii) agonist (claim 7), (iii) antagonist of a receptor (claim 7), or (iv) the polypeptide mimics the activity of a natural ligand (claim 11); or (C) screening as recited in each of claims 29-33. *Id.*, pages 5-6.

Additionally, with the election of Subgroup 2(A), if the interaction were with a cellular receptor, Applicants were further required to elect a single species of cellular receptor, specifically: (i) macrophage scavenger receptor (claim 8), (ii) cytokine receptor (claim 9), or (iii) chemokine receptor (claim 9). *Id.*, page 5. With the election of Subgroup 2(B)(i), Applicants were apparently further required to elect a species of a replicable genetic package: (a) bacteriophage (either gene II or gene VII), (b) cell, (c) spore, or (d) virus. *Id.*, pages 5-6.

With the election of Subgroup 3, Applicants were apparently further required to elect a species of "A. optimized products (of the composition)." *Id.*, page 6. With regard to these "optimized products," it appears that Applicants were required to elect one of the following:

- i. peptides or polypeptides; or
- ii. polynucleotides that encodes [*sic*]: (a) polynucleotide inserted into an antigen-encoding sequence of a genetic vaccine vector (claim 17); (b) polynucleotide that encodes an M-loop of an HBsAg polypeptide (claim 18); (c) rich in unmethylated CpG (claim 19); (d) encodes a peptide that inhibits an allergic reaction; (e) encodes a costimulator (claim 24); (f) encodes a cytokine antagonist (claim 36); or (g) encodes a polypeptide capable of inducing a predominantly Th1 immune response (claim 39) or Th2 response (claim 40). *Id.*, pages 6-7. Thus, if Subgroup 3 (A)(ii) were elected, one of (a)-(g) would also be required to be elected.

If Subgroup 3(A)(ii)(d) ("encodes a peptide that inhibits an allergic reaction") were elected, the Examiner further required that Applicants elect one of the following:

- i. interferon;
- ii. IL; or
- iii. antagonist of IL-4 or IL-5 or IL-13 or IL-10. (*Id.*, page 7.)

In addition, if IL-10 of Subgroup 3(A)(ii)(d)(iii) were elected, the Examiner appears to have further required election of one of the following:

1. soluble; or
2. defective IL-10 or IL-20/MDA-7. (*Id.*)

If Subgroup 3(A)(ii)(e) ("encodes a costimulator (claim 24)") were elected, the Examiner appears to have further required election of one of the following:

1. costimulator is B7-1;
2. B7-2 (claim 25);
3. CD1, CD40, CD154, CD150 (claim 36); or
4. cytokine (claim 27). (*Id.*)

It appears that if Subgroup 3(A)(ii)(e)(4) ("cytokine (claim 27)") were elected, Applicants were required to elect further "from claim 28 e.g., IL-1-18, GM-CSF etc." *Id.*

If Subgroup 3(A)(ii)(f) ("encodes a cytokine antagonist (claim 36)") were elected, Applicants were required to elect further one of the following:

- a. soluble cytokine receptor;
- b. transmembrane having a defective signal sequence; or
- c. IL-10 [*sic*] or -4R [*sic*] (claim 38). (*Id.*).

With the election of Group II, the Examiner required Applicants to elect one of the following: (A) "Method of creating a library of recombinant;" or (B) "Method of screening." The Examiner also required Applicants to elect a species of accessory molecule from one of the following: (A) proteasome or TAP (claim 43); (B) cytotoxic cell (claim 33); or (C) immunogenic agonist sequence (claim 46). *Id.*, page 8.

Applicants believe the species election requirement is moot in view of the addition of new claims 47-48 and cancellation of all pending claims 1-46. However, to the extent the species election requirement is found to apply to new claims 47 and 48 and is maintained in its present form, Applicants respectfully traverse the requirement for at least the following reasons.

Applicants respectfully submit that a *prima facie* case with regard to the species election requirement has not been made. To establish a *prima facie* case for a species election requirement, it must be shown, among other things, that the generic claim recites such a multiplicity of species that an unduly extensive and burdensome search would be required. In the present case, the Examiner has not shown with sufficient evidence or explanation that either of the previously pending claims found to be generic (claim 1 or claim 41) encompasses more than a reasonable number of species such that an unduly extensive and burdensome search would be necessary. On the contrary, Applicants submit that each of previously pending claims 1 and 41 included sufficiently few species such that a search and examination of all such species at one time would not pose a serious or undue burden on the Examiner.

Additionally, as noted above, the claims of the '258 patent issued to Short are substantially the same as those of previously pending claims 1-46, and Short claim 30 is essentially the same as new claims 47 and 48. The claims of the '258 patent were not subjected to a species election requirement. At the very least, the procedural treatment of the '258 patent suggests that a

search and examination of the species encompassed by previously pending claims 1 and 41 would not constitute an undue burden on the Examiner.

Moreover, Applicants believe that the species election requirement would not properly apply to new claims 47 and 48, as each of these claims includes sufficiently few species that a search and examination of all such species at one time would not pose a serious or undue burden on the Examiner.

For at least these reasons, Applicants respectfully submit that the species election requirement as to original claims 1-46 and/or new claims 47-48 is improper and furthermore does not properly apply to new claims 47 and 48.

However, in the event the species election requirement is found to apply to new claims 47 and 48 and is maintained in its present form, Applicants make the following provisional species election with traverse. Consistent with the provisional election of Claim Group I with traverse, as discussed above, for Subgroup 1, Applicants provisionally elect **Subgroup 1(c) "oligonucleotide-directed mutagenesis" with traverse**. Applicants submit no species election should be required for the method of creating a library as specified in step (a) of either of claims 47 and 48, because step (a) does not encompass more than a reasonable number of species and thus a search and examination of all such species at one time would not pose an undue burden on the Examiner. Such a provisional elections is being made for no other reason than to be viewed as fully responsive to the outstanding Restriction/Election Requirement and not as an admission that said election is at all necessary in view of canceled claims 1-46 and new claims 47-48.

With regard to Subgroup 2 ("screening method"), Applicants submit the screening method set forth in original claim 25 and new claims 47 and 48 (i.e., "*the screening step involves selecting variants with altered activity through CD28 or CTLA-4*"), encompasses only a reasonable number of species. The screening step of claims 47 and 48 parallels that of original claim 25. Thus, no unduly extensive or burdensome search would be required for original claim 25 or new claims 47 and 48. Consequently, no further election should be required. For at least these reasons, the election of species of screening method is traversed for original claim 25 and new claims 47 and 48. Applicants provisionally elect **"cellular receptor" corresponding to Subgroup 2(A)(a) with traverse**. Such a provisional elections is being made for no other reason than to be viewed as fully

responsive to the outstanding Restriction/Election Requirement and not as an admission that said election is at all necessary in view of canceled claims 1-46 and new claims 47 and 48.

With regard to the election of a species of cellular receptor, Applicants note that none of the designated species is directly applicable to original claim 25 or new claims 47 and 48, each of which specifies the *screening step involves selecting variants with altered activity through CD28 or CTLA-4*. Therefore, an appropriate election cannot be made. Moreover, original claim 25 and new claims 47 and 48 include only a reasonable number of species, and accordingly no unduly extensive or burdensome search would be required for these claims. Thus, no further election should be required. For at least these reasons, the election of species as pertains to the cellular receptor is traversed. Applicants provisionally elect **Subgroup2(A)(a)(ii) (“cytokine receptor”) with traverse**. Such a provisional election is being made for no other reason than to be viewed as fully responsive to the outstanding Restriction/Election Requirement and not as an admission that said election is at all necessary in view of canceled claims 1-46 and new claims 47 and 48.

With regard to Subgroup 3 (“composition of the optimized product or a method of administering”), Applicants submit the election as to the alleged composition has effectively been made by the submission of new claims 47 and 48, which specify the optimized recombinant polynucleotide encodes a costimulator selected from B7-1 or B7-2, or a B7-1 or B7-2 variant, respectively. As the new claims include only a reasonable number of species, no election should be required, since a unduly extensive or burdensome search would not be required. The same arguments can be applied to original claim 25, which includes parallel language. No further election should be required for original claim 25 or new claims 47-48. Nevertheless, Applicants provisionally elect **Subgroup 3(A)(ii)(e)(1) with traverse (“ii. polynucleotides that encodes:” [sic], “e. encodes a costimulator (claim 24)”, “1. costimulator is B7-1.”)** Such a provisional elections is being made for no other reason than to be viewed as fully responsive to the outstanding Restriction/Election Requirement and not as an admission that said election is at all necessary in view of canceled claims 1-46 and new claims 47 and 48.

New claims 47 and 48 are readable upon the elected species.

In the event the species election requirement is made final, Applicants respectfully reserve the right to petition the Commissioner to review the requirement.

III. 35 U.S.C. § 135(B) IS SATISFIED

As discussed during the interview, at least one claim is being submitted in the above-referenced application which is the same as, or for the same or substantially the same subject matter as, a claim of the '258 patent (*e.g.*, claim 30). The new claims are being submitted prior to one year from the date on which the '258 patent was granted (*i.e.*, November 12, 2002). Thus, 35 U.S.C. § 135(b) is satisfied.

IV. HANDLING THIS APPLICATION WITH SPECIAL DISPATCH

The Manual of Patent Examining Procedure (MPEP) states at § 708.01 that:

The following is a list of special cases (those which are advanced out of turn for examination):

(F) Applications ... which will be placed in interference with an unexpired patent or patents.

Reference should also be made to MPEP § 2307, under the heading "SPECIAL DISPATCH", which states:

Examiners should note that 37 CFR 1.607 requires that examination of an application in which applicant seeks an interference with a patent "shall be conducted with special dispatch."

See MPEP § 708.01.

Since Applicants are requesting an interference with an unexpired patent, examination of the current application should be handled with special dispatch. Applicants are in the process of finalizing their Request for Interference with the '258 patent, as discussed during the interview. However, since the first step is a determination of the patentability of Applicants' claims, examination should proceed prior to receipt of that Request.

CONCLUSION

Accordingly, for at least all of the reasons set forth above, withdrawal of the requirement for restriction and species election, to the extent they apply to new Claims 47 and 48, if at all, is requested.

In view of the foregoing, Applicants believes all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If there are any questions concerning this paper, or the application in general, the Examiner is invited to telephone the undersigned at (650) 298-5809 at her earliest convenience.

Respectfully submitted,

A handwritten signature in cursive script, appearing to read "Margaret A. Powers".

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APPENDIX A

**"MARKED UP" PARAGRAPHS ILLUSTRATING THE AMENDMENTS MADE TO THE
SPECIFICATION OF 09/724,869 WITH ENTRY OF THIS AMENDMENT**

Paragraph beginning on page 1, line 6:

This application is a continuation of US Patent Application Serial No. 09/248,716, filed February 10, 1999, which [and] claims the benefit of US Provisional Application Serial No. 60/074,294 [60/074], filed February 11, 1998, which applications are incorporated herein by reference for all purposes.

